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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,498	11/21/2005	Gabriella Minchiotti	1118-PCT-US	8348

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EXAMINER	
GAMETT, DANIEL C	
ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,498	MINCHIOTTI ET AL.	
	Examiner	Art Unit	
	DANIEL C. GAMETT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 20-22* is/are pending in the application.

4a) Of the above claim(s) *13-18 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/20/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of claims 1-12 in the reply filed on 10/29/2008 is acknowledged. The traversal is on the ground(s) that claims 1-18 and 20-22, Group I and Group II are drawn to one of the combinations of categories specified in 37 C.F.R. 1.475(b) to be considered to have unity of invention, specifically a "product, a process specially adapted for the manufacture of the said product, and a use of the said product". This is not found persuasive because the groups of claims are not drawn to a single product or related groups of products and processes. The products recited in Group I include a protein of the EGF-CFC family and cardiomyocytes differentiated from stem cells; the recited processes are cardiomyocyte differentiation of stem cells and treatment of heart diseases. In Group II, the recited products are an inhibitor of Cripto and neuronal cells differentiated from stem cells; the recited processes are neuronal differentiation of stem cells and treatment of neuropathologies.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 13-18 and 20-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/29/2008.

3. Claims 1-12 are under consideration.

Claim Rejections - 35 USC § 101 and § 112

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 8 provides for the use of stem cells according to claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

8. Claim 8 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in

the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

11. Claims 9-12 are drawn to compositions for therapeutic use for treating heart disorders that comprises a therapeutically effective amount of a protein or its derivative, having at least the EGF and CFC domains of a protein of the EGF-CFC family.

12. The courts have interpreted the first paragraph of 35 U.S.C. 112 to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971).

13. In the present case, it has not been established that Cripto, or any protein having at least the EGF and CFC domains of a protein of the EGF-CFC family, has any effect on cardiogenesis in post-natal mammals—the known effects are confined to early embryonic development. There is no basis for expecting that one of skill in the art could make and use a therapeutic composition that comprises a protein having at least the EGF and CFC domains of a protein of the EGF-CFC family for treating heart disorders regardless of how much experimentation the skilled artisan might be willing to perform.

14. The courts have stated that patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute an enabling disclosure. Reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. See *Genentech v. Novo Nordisk A/S* (CAFC) 42 USPQ2d 1001 (1997). Further, as stated in

Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005), "If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/68814, published September 20, 2001 (of record). The instant claims are drawn to cardiomyocytes that have been produced by differentiation of stem cells and to composition and methods of their therapeutic use. WO 01/68814 cites (see page 5) earlier work which shows that embryonic stem cells differentiate in vitro to produce functional cardiomyocytes. Such cardiomyocytes are

indistinguishable from the cardiomyocytes of the instant claims. The courts have established that if a claimed product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe.,* 227 USPQ 964, 966 (Fed. Cir. 1985): *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983). WO 01/68814 further teaches the therapeutic administration of cardiomyocytes derived from stem cells (see Examples 3 and 4 p.32-33; claim 41), thereby anticipating the composition and method of instant claims 7 and 8.

17. Claims 6-8 are rejected under 35 U.S.C. 102(e) as being anticipated by US 7425448, filed July 12, 2002. The '448 patent teaches a system for the production of human cardiomyocytes from human embryonic stem cells. The resultant cardiomyocytes are indistinguishable from the cardiomyocytes of instant claim 6. The courts have established that if a claimed product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe.,* 227 USPQ 964, 966 (Fed. Cir. 1985): *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983). The '448 patent teaches therapeutic administration of the cells (column 20, line 46-column 21, line 67) thereby anticipating the composition and method of instant claims 7 and 8.

18. Claims 1, 2, and 4-6 are rejected under 35 U.S.C. 102(b) as being anticiapted by Xu *et al.,* Developmental Biology 1998 Apr 15;196(2):237-247 (of record). Xu *et al*. disclose that cripto double "knockout" Cr(-/-) mouse ES cells that have selectively lost the ability to form beating cardiac myocytes can be rescued by reintroducing Cr-1 gene back into the Cr(-/-) cells

(see Abstract). Xu *et al.*, therefore practiced a method to induce stem cell differentiation in cardiomyocytes wherein the cells are exposed for a period of time and in effective amounts to a protein of the EGF-CFC family or its derivatives, which comprises at least the EGF and CFC domains derived from the mouse cripto protein, wherein cell exposure occurs through genetic expression in stem cells via a suitable vector, as recited in claim 1, 2, 4, and 5. The rescued cardiomyocytes are indistinguishable from the cardiomyocytes of instant claim 6.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Xu *et al.,* Developmental Biology 1998 Apr 15;196(2):237-247 as applied to claim 1, 2, 4, and 5 above, and further in view of US 7425448, filed July 12, 2002. As noted, Xu *et al.*, teaches the method recited in claims 1, 2, 4, and 5, wherein stem cells are induced to differentiate into cardiomyocytes by the introduction of mouse cripto through genetic expression in stem cells via a suitable vector. Xu *et al.* do not, however, teach the same method using human Cripto, as required in claim 3. Also as noted above, the '448 patent teaches a system for the production of human cardiomyocytes from human embryonic stem cells. The '448 patent teaches that the cells

can also be genetically altered in order to express one or more growth factors of various types, specifically including cripto (column 18, lines 30-44). The '448 patent, therefore, provides motivation and expectation of success for one of skill in the art to introduce human cripto into human cells to achieve effects similar to those observed by Xu *et al.* with mouse reagents, thereby arriving at the method recited in instant claim 3. Therefore, the method recited in instant claim 3 is prima facie obvious in view of the combined teachings of the cited references.

Conclusion

21. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C. Gamett, PhD., whose telephone number is (571)272-1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571 272 0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel C Gamett/
Examiner, Art Unit 1647